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**Patent and Trademark Office**

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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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MINNIFIELD EXAMINER

18N1/1101

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ART UNIT PAPER NUMBER

1802

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DATE MAILED: 11/01/95

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on \_\_\_\_\_ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.  
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ \_\_\_\_\_

**Part II SUMMARY OF ACTION**

1. ☒ Claims 1-38 are pending in the application.  
Of the above, claims 1-17, 20-33, 35-36 are withdrawn from consideration.

2. ☐ Claims \_\_\_\_\_ have been cancelled.

3. ☐ Claims \_\_\_\_\_ are allowed.

4. ☒ Claims 18-19, 34, 37, 38 are rejected.

5. ☐ Claims \_\_\_\_\_ are objected to.

6. ☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on \_\_\_\_\_. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on \_\_\_\_\_, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed \_\_\_\_\_, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. \_\_\_\_\_; filed on \_\_\_\_\_.

13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

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### **Part III DETAILED ACTION**

15. Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group I. Claims 1-17, 20-23, 29, 30, 35 and 36 drawn to DNA, classified in Class 536, subclass 22.1, 23.1 and 23.7.

Group II. Claims 18, 19, 37 and 38, drawn to polypeptides and antibodies, classified in Class 530, subclass 387.1, 388.1, 389.1, 389.5, 300, 350 and 328.

Group III. Claims 24-28 and 31-34, drawn to host cells with mutant genes, classified in Class 435, subclass 252.3, 172.1 and 172.3.

The inventions are distinct, each from the other because of the following reasons:

The claimed inventions are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case infection due to *H. pylori* can be treated with other compounds or compositions other than the composition containing the presently claimed polypeptide or antibody. Further, the products can be used in diagnostic testing.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and the search required for one Group is not required for another Group, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

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During a telephone conversation with David Vance on March 3, 1995 a provisional election was made with traverse to prosecute the invention of Group II. Affirmation of this election must be made by applicant in responding to this Office action. Claims 1-17, 20-36 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

16. Acknowledgment is made of applicant's claim for priority based on an patent from France, 9112198 issued 10-03-91. It is noted, however, that applicant has not filed a certified copy of the foreign patent, English translation, as required by 35 U.S.C. § 119. See MPEP 201.14(a). Applicants' effective file date is 10-02-92.

17. The disclosure is objected to because of the following informalities: On page 39, table 2, the footnotes are incomplete; footnote (1) and (5) are explained however they are not denoted in the table. Appropriate correction is required.

18. Claim 37 is rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The product (polyclonal antibody), as claimed, has the same characteristics and utility as that found in nature because these antibodies are produced in nature. To overcome this rejection the Examiner suggests the amendment of the claims to include purity limitations which would distinguish the characteristics and utility of applicant's product as enabled in the specification from the utility of the product as it exists in nature. It is further suggested that such limitation

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include the terminology "essentially purified and isolated" (i.e. if such purity is supported in the specification) and/or a description of what applicant's protein is "free of" relative to the natural source which imparts a distinct utility to the claimed product. For relevant case law see Farbenfabriken of Elberfeld Co. v. Kuehmsted, 171 Fed. 887, 890 (N.D. Ill. 1909) (text of claim at 889); Parke-Davis & Co. v. H.D. Mulford Co., 189 Fed. 95, 103, 106, 965 (S.D.N.Y. 1911) (claim 1); and In re Bergstrom, 427 F.2d 1394, 1398, 1401-1402 (CCPA 1970).

19. The following is a quotation of the first paragraph of 35 U.S.C. § 112: The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention. The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure. The claims, 37 and 38, are directed to antibodies, and compositions to treat infection due to *H. pylori*. However, the specification is not enabled for nor has taught one of skill in the art how to obtain these antibodies and compositions to treat infection due to *H. pylori*. It is noted that the art teaches that "[W]ith the exception of UreA and UreB structural polypeptides of the enzyme, no role can as yet be assigned to the nine proteins encoded by the *H. pylori* urease gene cluster." (Cussac et al. 1992, abstract). Therefore it is unclear how the products, polypeptides, from these genes can be used in compositions to treat infection due to *H. pylori*. Further, Houghten et al. teach that changes/modifications (addition, substitution, deletion or inversion) of one or more amino acids in a polypeptide will alter antigenic determinants and therefore effect antibody production (p. 21). Houghten et al. also teach that "... combined effects of multiple

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changes in an antigenic determinant could result in a loss of [immunological] protection." and "A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies..." (p. 24). It is not always possible to make antibodies or protect against infection if the antigenic determinants have been altered. Applicants propose to make recombinant strains using mutations in the Ure genes and then use these in compositions, however as set forth above it is unclear if changes/modifications that occur in the gene will effect the antigenic determinants; i.e. are the determinants maintained in order to obtain a composition. Further, the antigenic determinants or epitopes have not been disclosed for the *H. pylori* urease. The specification has not taught the use of fragments; how to obtain these fragment or how much of the polypeptide constitutes a fragment. What is the minimal portion that is needed for the polypeptide to remain functional? In view of the reasons set forth, there would be undue experimentation for a skilled artisan to practice the claimed invention.

20. Claims 37 and 38 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

21. Claims 18, 19, 37 and 38 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are rejected as failing to define the invention in the manner required by 35 U.S.C. § 112, second paragraph. The claims are narrative in form and replete with indefinite and functional or operational language. The structure which goes to make up the device must be clearly and positively specified. The structure must be organized and correlated in such a manner as to present a complete operative device. The claims must be in one sentence form only. Note the format of the claims in the patent cited (Rashtchian et

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al.). The claims are indefinite for being in improper Markush format. The Office recommends the use of the phrase "selected from the group consisting of..." with the use of the conjunction "and" rather than "or" in listing the species. See MPEP 706.03(Y). The use of the phrase "for example" renders claim 18 indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention or not, and the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. The phrase "such as" renders the claim 19 indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention or not, and the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Claim 19 is vague and indefinite in the recitation an alternative expression, "and/or", wherein the limitation covers two different elements, i.e. regulation is not the same as maturation. See MPEP 706.03(d), paragraph 5. Claim 38 lacks positive antecedent basis in the recitation of "antibody". Claims 18 and 19 are vague and indefinite in the recitation of "corresponds", because it is unclear what is intended.

22. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

23. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention

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was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

24. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

25. Claims 18 and 19 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Mulrooney et al., Ferrero et al., Bradley et al. or Tabaqchali et al.

Mulrooney et al. disclose polypeptides encoded by the UreE, UreF and UreG (abstract). Mulrooney et al. disclose that these genes are accessory genes in urease activity (abstract; p. 5839). Ferrero et al. disclose Ure genes from *H. pylori* and the expression of these genes in *C. jejuni* or *E. coli* (abstract). Bradley et al. disclose Ure genes, UreE and UreF, that encode for polypeptides (abstract; materials and methods). Tabaqchali et al. disclose nucleotide sequences characterized in that it comprises a part of the nucleic sequence (2622-2693) corresponding to the gene known as UreI.

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The prior art, Mulrooney et al., Ferrero et al., Bradley et al. or Tabaqchali et al., discloses polypeptides, which appears to be the same as the claimed invention. Therefore, the prior art polypeptides appear to be the same, with any other identifying characteristics inherent in them. The art anticipates the claimed invention because the claims recite any part of the claimed sequence; it covers virtually any portion of the amino acid sequence.

And if the prior art products, polypeptides, are not the same as that claimed, they are obvious variations of that claimed, which the teachings of the prior art would have reasonably suggested to one of ordinary skill in the art at the time the invention was made, to use the disclosed genes to express the claimed polypeptides, making the claimed invention, as a whole prima facie obvious to one of ordinary skill in the art at the time the invention was made. It would have been obvious to a person of ordinary skill in the art at the time the invention was made that the polypeptide corresponding to the sequence disclosed in the art can easily be derived.

Since the Office does not have the facilities for examining and comparing applicants' disclosed polypeptides and the disclosed polypeptides of the prior art the burden is on applicant to show a novel or unobvious differences between the claimed polypeptide and the disclosed polypeptides of the prior art (i.e., that the disclosed polypeptides of the prior art does not possess the same material structural and functional characteristics of the claimed polypeptides). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

26. Claims 37 and 38 are rejected under 35 U.S.C. § 103 as being unpatentable over Mulrooney et al., Ferrero et al., Bradley et al. or Tabaqchali et al. as applied to claims 18 and 19 above, and further in view of Sevier et al..

Mulrooney et al. disclose polypeptides encoded by the UreE, UreF and UreG (abstract). Mulrooney et al. disclose that these genes are accessory genes in urease activity (abstract; p. 5839). Ferrero et al. disclose Ure genes from *H. pylori* and the

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expression of these genes in *C. jejuni* or *E. coli* (abstract). Bradley et al. disclose Ure genes, UreE and UreF, that encode for polypeptides (abstract; materials and methods). Tabaqchali et al. disclose nucleotide sequences characterized in that it comprises a part of the nucleic sequence (2622-2693) corresponding to the gene known as UreI. Sevier et al. teach the use of antibodies for immunodiagnostics or immunotherapy (abstract; p. 1800; 1802). It would have been obvious to a person of ordinary skill in the art the time the invention was made to use the polypeptides as taught in the prior art with the expectation of obtaining antibodies to the claimed polypeptides. Further, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the polypeptides in a composition to treat infection due to *H. pylori* since Ferrero et al. teach that these polypeptides can "...be useful in animal model for addressing the role of urease in the establishment and the maintenance of *H. pylori* infection." (abstract). The claimed invention is prima facie obvious in view of the teachings of Mulrooney et al., Ferrero et al., Bradley et al. or Tabaqchali et al. taken with Sevier et al., absent any convincing evidence to the contrary.

27. No claims are allowed.

28. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is (703) 305-3394. The examiner can normally be reached on Monday-Thursday from 7:00 AM-4:30 PM. The examiner can also be reached on alternate Fridays.

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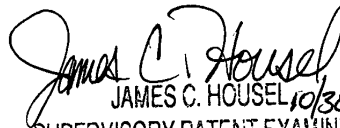
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is (703) 305-7939.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

N. M. Minnifield  
October 26, 1995

  
JAMES C. HOUSEL 10/30/95  
SUPERVISORY PATENT EXAMINER  
GROUP 180